UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/744,641 | 07/27/2001 | Marc Pignot | 11413-003001 | 3092 |

7590 04/07/2003

Fish & Richardson
4350 La Jolla Village Drive Suite 500
San Diego, CA 92122

| EXAMINER | |
|---|---|
| YOUNG, JOSEPHINE | |
| **ART UNIT** | **PAPER NUMBER** |
| 1623 | 13 |

DATE MAILED: 04/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Offic Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/744,641 | PIGNOT ET AL. | |
| | Examiner | Art Unit | |
| | Josephine Young | 1623 | |

*-- The MAILING DATE of this c mmunication appears on the cover sheet with the c rrespondence address --*

**P ri d for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *24 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *16-19,21-26 and 28-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15 and 20-27* is/are rejected.

7)☒ Claim(s) *16-19,21-26 and 28-30* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Pri rity under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

### *Election/Restrictions*

Applicant's election with traverse of Group I in Paper No. 12, mailed December 24, 2002, is acknowledged.

The restriction requirement made in Paper No. 10, mailed September 26, 2002 is hereby withdrawn. As such, claims 9-14, 16-30 are rejoined.

### *Claim Objections*

Claims 16-19, 21-26 and 28-30 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. See MPEP § 608.01(n). Accordingly, claims 16-19, 21-26 and 28-30 have not been further treated on the merits.

### *Claim Rejections - 35 USC § 101*

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 20-26 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd. App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

***Claim Rejections - 35 USC § 112, First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Undue experimentation is a conclusion reached by weighing the noted factual considerations set forth below in In re Wands USPQ2d 14000. A conclusion of lack of enablement means that, based on the evidence regarding a fair evaluation of an appropriate combination of the factors below, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention.

These factors include

(1) quantity of experimentation necessary,

(2) the amount of guidance presented,

(3) the presence or absence of working examples,

(4) the nature of the invention,

(5) the state of the prior art,

(6) the predictability of the art and

(7) the breath of the claims.

Further, claims 1-15 and 27 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the compounds of the formula 2 and 9 on page 12 and 16

of the specification, respectively, i.e. wherein X is N, Y is N, $R^2$ is H and n is 1-4, does not reasonably provide enablement for the broad genus of compounds of formula (I), and in particular for compounds wherein X is not N, Y is not N, $R^2$ is not H and n is up to 5000. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

With regard to factors (1) and (2) cited above, undue experimentation is required to determine how to make and use compounds other than compounds of the formula 2 and 9 on page 12 and 16 of the specification, respectively, i.e. to synthesize the aziridine derivative and to determine if such derivative is a cofactor for a S-adenosyl-L-methionine (SAM) dependent methyltransferase, for which the instant invention is applicable. There has not been provided adequate guidance in the written description for accomplishing such, as only two different aziridine analogs were synthesized, out of the limitless analogs encompassed within the broad genus.

With regard to factors (4), (5) and (6), it is noted that there is a great deal of unpredictability in the art. For example, there is no synthetic method that can be broadly applied to linking a group comprising one methylene chain as well as linking a group comprising 5000. Further, the three-dimensional structure of several methyltransferases in complex with the natural cofactor have indicated that the 8-position of the adenine ring of the natural cofactor is at least partly assessable to solvent. However, in some methyltransferases, the 7-position of the adenine ring is more exposed to the solvent. Therefore, the art fails to definitely establish a pattern between derivations in the 7 or 8 position and specificity for a broad class of

methyltransferases. The art at the time the invention was made fails to establish predictability with regard to how to make and use the aziridine derivatives as instantly claimed.

With regard to factors (3) and (7), it is noted that while there are two working examples of how to make and use particular aziridine derivatives, it is not seen as sufficient to support the breath of the claims. It is noted that Law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves. See In re Gardner et al. 166 USPQ 138 (CCPA 1970).

Further, claims 9-10 and 13 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the complexes with DNA methyltransferases, such as M·Taq1 and M·Hha1, does not reasonably provide enablement for the broad genus of methyltransferases, such as polypeptide, protein, enzyme or small molecule methyltransferases, as instantly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

With regard to factors (1) and (2) cited above, undue experimentation is required to determine which specific methyltransferase would be able to complex with a particular aziridine derivative of the present invention. There has not been provided adequate guidance in the written description for accomplishing such, as only as only two different aziridine analogs were synthesized and complexed with the DNA methyltransferases, M·Taq1 and M·Hha1, out of the limitless analogs encompassed within the broad genus, and numerous methyltransferases known in the art.

With regard to factors (4), (5) and (6), it is noted that there is a great deal of unpredictability in the art. For example, the three-dimensional structures of several methyltransferases in complex with the natural cofactor have indicated that the 8-position of the adenine ring of the natural cofactor is at least partly assessable to solvent. However, in some methyltransferases, the 7-position of the adenine ring is more exposed to the solvent. Therefore, the art fails to definitely establish a pattern between derivations in the 7 or 8 position and specificity for a broad class of methyltransferases. The art at the time the invention was made fails to establish predictability with regard to how to make and use the complex of the aziridine derivatives with any methyltransferase as instantly claimed.

With regard to factors (3) and (7), it is noted that while there are two working examples of complexes with two different DNA methyltransferases, it is not seen as sufficient to support the breath of the claims. It is noted that Law requires that the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not how to find out how to use it for themselves. See In re Gardner et al. 166 USPQ 138 (CCPA 1970).

### *Claim Rejections - 35 USC § 112, Second Paragraph*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 and 20-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 20-26 provides for the use of the compound of any one of claims 1 to 8, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

The phrase "amino acids which may optionally be modified" in claim 1 renders the claims in which it appears indefinite. In the absence of the specific modification to the amino acid or distinct language to describe the structural modifications or the chemical names of the modified amino acid of this invention, the identity of said optionally modified amino acids would be difficult to describe and the metes and bounds of said optionally modified amino acids that Applicant regards as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claims.

Similarly, the term "derivatives thereof" in claim 4 and "a derivative thereof or an aldehyde derivative" in claim 7 renders the claims in which it appears indefinite. In the absence of the specific derivation or distinct language to describe the structural derivatives or the chemical names of the derivatives of this invention, the identity of said derivative would be difficult to describe and the metes and bounds of said aziridine derivative that Applicant regards as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claims.

The term "electron withdrawing group" in claim 1 renders the claims in which it appears indefinite. In the absence of a particular electron withdrawing group or distinct language and/or chemical formula to describe class of compounds that would be considered an electron withdrawing group of this invention, the identity of said electron withdrawing group would be

difficult to describe and the metes and bounds of said aziridine derivative that Applicant regards as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claims.

The term "small molecule" in claim 10 renders the claims in which it appears indefinite. In the absence of a particular small molecule or distinct language and/or chemical formula to describe class of compounds that would be considered a small molecule of this invention, the identity of said small molecule would be difficult to describe and the metes and bounds of said methyltransferase that Applicant regards as the invention cannot be sufficiently determined because they have not been particularly pointed out or distinctly articulated in the claims.

***Prior Art***

Claims 1-15 and 27 appear to be free of the prior art. The closest prior art references are considered to be patent no. US 5,610,289 to COOK et al. and patent publication WO 88/09796 to GENENTECH, INC.

COOK teaches backbone modified oligonucleotide analogs, wherein the backbone can be modified with ethylaziridine or substituted ethylaziridine ring. See column 5, line 1 to column 6, line 9, and in particular column 6, lines 5-7. However, COOK does not teach aziridine derivatives of the present invention.

GENENTECH teaches fused and 3'-spiro aziridine nucleoside analogs. See page 3, lines 10-29. However, GENENTECH does not teach the 5'-aziridine nucleoside analogs of the present invention.

Therefore, claims 1-15 and 27 would be allowable if rewritten or amended to overcome the rejection(s) under 35 U.S.C. 112, first and second paragraphs, set forth in this Office action.

***Conclusion***

Claims 1-30 are pending. Claims 16-19, 21-26 and 28-30 are objected to and withdrawn. Claims 1-15 and 20-27 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Josephine Young whose telephone number is (703) 605-1201. The examiner can normally be reached on Monday through Friday, 9:00 a.m. to 6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached at (703) 308-4624. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.

JY
April 4, 2003

JAMES O. WILSON
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600